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Kiyotaka [JP/JP]; Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **MAEDA, Masashi** [JP/JP]; Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **SATO, Natsuki** [JP/JP]; Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).

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(54) Title: **NEW USE**

(57) Abstract: The present invention is related to a new use of a plasminogen activator, for increasing an effect caused by IL-2 inhibitor and, further, a use of IL-2 inhibitor for increasing or decreasing an effect caused by plasminogen activator.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 00/06874

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/39 //(A61K38/39, 31:445)

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According to International Patent Classification (IPC) or to both national classification and IPC

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>MAEDA MASASHI ET AL: "FK506 (tacrolimus) as a potential anti-stroke agent (3): Increased therapeutic efficacy with combined treatment of FK506 and recombinant tissue plasminogen activator (rt-PA) in a rat stroke model." JAPANESE JOURNAL OF PHARMACOLOGY, vol. 82, no. Suppl. 1, 2000, page 174P XP000990982</p> <p>73rd Annual Meeting of the Japanese Pharmacological Society.; Yokohama, Japan; March 23-25, 2000 ISSN: 0021-5198 * See Abstracts P217-P219, and in particular P218 *</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	<p>1-15</p> <p style="text-align: right;">RECEIVED</p> <p style="text-align: right;">APR 15 2003</p> <p style="text-align: right;">TECH CENTER 1600/2900</p>



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

Int. l. Application No

PCT/JP 00/06874

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>YAGITA Y ET AL: "EFFECT OF IMMUNOSUPPRESSANT FK506 ON ISCHEMIA-INDUCED DEGENERATION OF HIPPOCAMPAL NEURONS IN GERBILS"</p> <p>LIFE SCIENCES, PERGAMON PRESS, OXFORD, GB, vol. 59, no. 19, 1996, pages 1643-1650, XP000980211</p> <p>ISSN: 0024-3205</p> <p>the whole document</p>	1-15
Y	<p>TOUNG THOMAS J ET AL: "Neuroprotective FK506 does not alter in vivo nitric oxide production during ischemia and early reperfusion in rats."</p> <p>STROKE, vol. 30, no. 6, June 1999 (1999-06), pages 1279-1285, XP000980399</p> <p>ISSN: 0039-2499</p> <p>the whole document</p>	1-15
Y	<p>BOCHELEN D ET AL: "CALCINEURIN INHIBITORS FK506 AND SDZ ASM 981 ALLEVIATE THE OUTCOME OF FOCAL CEREBRAL ISCHEMIC/REPERFUSION INJURY"</p> <p>JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, AMERICAN SOCIETY FOR PHARMACOLOGY AND, US, vol. 288, no. 2, February 1999 (1999-02), pages 653-659, XP000980203</p> <p>ISSN: 0022-3565</p> <p>the whole document</p>	1-15
Y	<p>KIM YANG-HEE ET AL: "Nonproteolytic neuroprotection by human recombinant tissue plasminogen activator."</p> <p>SCIENCE (WASHINGTON D C), vol. 284, no. 5414, 23 April 1999 (1999-04-23), pages 647-650, XP002164663</p> <p>ISSN: 0036-8075</p> <p>the whole document</p>	1-15
Y	<p>BEDNAR M M ET AL: "COMBINATION TISSUE PLASMINOGEN ACTIVATOR AND TICLOPIDINE THERAPY IN A RABBIT MODEL OF ACUTE THROMBOEMBOLIC STROKE"</p> <p>NEUROLOGICAL RESEARCH, XX, XX, vol. 18, no. 1, 1 February 1996 (1996-02-01), pages 45-48, XP000646532</p> <p>the whole document</p>	1-15
Y	<p>US 5 945 432 A (BEDNAR MARTIN M ET AL)</p> <p>31 August 1999 (1999-08-31)</p> <p>the whole document</p>	1-15

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 00/06874

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 648 351 A (KELLY JOHN S ET AL) 15 July 1997 (1997-07-15) the whole document ---	1-15
A	BUNDICK ET AL: "FK506 AS AN AGONIST TO INDUCE INHIBITION OF INTERLEUKIN 2 PRODUCTION" TRANSPLANTATION,US,WILLIAMS AND WILKINS, BALTIMORE, MD, vol. 53, no. 5, 1992, pages 1150-1153, XP000913592 ISSN: 0041-1337 the whole document -----	1-15

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Continuation of Box I.2

Present claims 1-15 relate to a rather large number of possible compounds, which are defined by reference to pharmacological mechanisms of action: The expression: "use of a plasminogen activator for manufacturing a medicament for increasing an effect caused by IL-2 inhibitor" in claim 1 and "use of IL-2 inhibitor for manufacturing a medicament for increasing or decreasing the effect caused by plasminogen activator" in claim 12 defines compounds by reference to pharmacological mechanisms of action; in the present context this wording is considered to lead to a lack of clarity within the meaning of Art. 6 PCT. It is impossible to fully compare the parameters the applicant has chosen to employ with what is set out in the prior art.

Support and/or disclosure within the meaning of Articles 5,6 PCT is to be found however for only a very small proportion of the compounds claimed. Consequently, the search has been carried out for those parts of the claims which appear to be clear, concise, supported and disclosed, namely for the combined, simultaneous, separate or sequential use of FK506 or cyclosporine, and tissue-type plasminogen activator (t-PA,) in relation to a neuroprotective therapy, for the treatment and the prevention of neurodegenerative diseases, and cerebral ischemic diseases, with due regard to the general idea underlying the application.

All claims 1 to 15 have been searched incompletely.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 00/06874

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5945432	A	31-08-1999	NONE	
US 5648351	A	15-07-1997	AU 687025 B	19-02-1998
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			JP 8505136 T	04-06-1996
			JP 3038920 B	08-05-2000